Express Mail Label No.: EV923350534US
Date of Deposit: July 18, 2007

Attorney Docket No. 24024-506 CON
GE Ref.: 26736

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS : Peled et al.
SERIAL NUMBER : 10/767,064 EXAMINER : Anoop Kumar Singh
FILING DATE : January 29, 2004 ART UNIT : 1632
FOR : EX-VIVO EXPANSION OF HEMATOPOIETIC STEM CELL POPULATIONS IN MONONUCLEAR CELL CULTURES

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

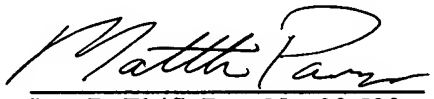
TRANSMITTAL LETTER

Enclosed herewith for filing in the above-identified application please find the following documents:

1. Amendment and Response to January 18, 2007 Office Action (19 pgs.);
2. Abstract (Cytotherapy 2004;6:344-355) (1 pg.);
3. Petition for Extension of Time (1 pg.);
4. Check No. 24436 in the amount of $510.00 to cover the Extension fee;
5. Return Postcard.

The Commissioner is hereby authorized to charge payment of any additional fees required in connection with the papers transmitted herewith, or credit any overpayment of same, to Deposit Account No. 50-0311, (Reference No. 24024-506 CON). A duplicate copy of this Transmittal Letter is enclosed.

Respectfully submitted,



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Dated: July 18, 2007

1: Cytotherapy. 2004;6(4):344-55.

Pre-clinical development of cord blood-derived progenitor cell graft expanded ex vivo with cytokines and the polyamine copper chelator tetraethylenepentamine.

- Peled T,
- Mandel J,
- Goudsmid RN,
- Landor C,
- Hasson N,
- Harati D,
- Austin M,
- Hasson A,
- Fibach E,
- Shpall EJ,
- Nagler A.

Gamida-Cell Ltd, Jerusalem, Israel.

BACKGROUND: We have previously demonstrated that the copper chelator tetraethylenepentamine (TEPA) enables preferential expansion of early hematopoietic progenitor cells (CD34+CD38-, CD34+CD38-Lin-) in human umbilical cord blood (CB)-derived CD34+ cell cultures. This study extends our previous findings that copper chelation can modulate the balance between self-renewal and differentiation of hematopoietic progenitor cells. METHODS: In the present study we established a clinically applicative protocol for large-scale ex vivo expansion of CB-derived progenitors. Briefly, CD133+ cells, purified from CB using Miltenyi Biotec's (Bergisch Gladbach, Germany) CliniMACS separation device and the anti-CD133 reagent, were cultured for 3 weeks in a clinical-grade closed culture bag system, using the chelator-based technology in combination with early-acting cytokines (SCF, thrombopoietin, IL-6 and FLT-3 ligand). This protocol was evaluated using frozen units derived from accredited cord blood banks. RESULTS: Following 3 weeks of expansion under large-scale culture conditions that were suitable for clinical manufacturing, the median output value of CD34+ cells increase by 89-fold, CD34+CD38- increase by 30-fold and CFU cells (CFUc) by 172-fold over the input value. Transplantation into sublethally irradiated non-obese diabetic (NOD/SCID) mice indicated that the engraftment potential of the ex vivo expanded CD133+ cells was significantly superior to that of unexpanded cells: 60+/-5.5% vs. 21+/-3.5% CD45+ cells, P=0.001, and 11+/-1.8% vs. 4+/-0.68% CD45+CD34+ cells, P=0.012, n=32, respectively. DISCUSSION: Based on these large-scale experiments, the chelator-based ex vivo expansion technology is currently being tested in a phase 1 clinical trial in patients undergoing CB transplantation for hematological malignancies.

PMID: 16146887 [PubMed - indexed for MEDLINE]